

**Amendments to the Specification:**

Please replace the paragraph at page 1, lines 8-9 of the specification with the following substitute paragraph:

This application claims priority under 35 U.S.C. §119 ~~based upon~~ to U.S. provisional Patent Application No. 60/203,271, filed May 10, 2000.

Please replace the paragraph at page 1, lines 14-20 of the specification with the following substitute paragraph:

The present invention generally relates to the fields of oncology, biochemistry, and immunology and to methods of early diagnosis of precancerous or cancerous conditions in a mammal and, more particularly, to a method of diagnosing precancerous or cancerous conditions in a mammal, wherein a biological sample is obtained from ~~said a~~ gastrointestinal site of said mammal to detect the presence of a backleak of signature proteins or carbohydrates indicating tight junctional leakiness at an early stage of a cancerous or precancerous condition.

Please replace the paragraph at page 3, lines 9-20 of the specification with the following substitute paragraph:

Tight junctional leakiness between gastrointestinal epithelia in the vicinity of the secretion of these proteins, or downstream of their secretion, will allow for their chronic leak into the

bloodstream, raising their level in serum. Therefore, salivary amylase levels in serum have important diagnostic predictive value for esophageal and gastric precancerous conditions, specifically Barrett's Esophagus, atrophic gastritis and H. pylorii infection. Serum pepsin levels likewise have diagnostic value in precancerous gastric conditions, such as atrophic gastritis and H. pylorii infection. The secretion of TFF3 (ITF) in the lower intestine and colon makes its serum level predictive of precancerous leaks in the ileum and colon. For all three markers, elevated serum levels of these proteins can serve as low cost, noninvasive indicators whose presence can alert the physician to the need for the more expensive and involved endoscopic or colonoscopic follow-up procedures.

Please replace the paragraph at page 5, lines 12-20 of the specification with the following substitute paragraph:

Using the same methods with which tight junctional leakiness was observed in tumor epithelia of human colon, tissue is ~~now~~ obtained (by gastrectomy) from patients undergoing stomach surgery for adenocarcinoma. Where the tumor is large enough to permit taking a portion for research purposes, samples are taken ~~off~~ from histologically normal mucosa and from the edge of the excised tissue alongside portions of mucosa from the very edge of the tumor. Comparative permeability determinations are made electrophysiologically, by radiotracer flux and by use of electron dense dyes in electron microscopy, all

techniques which have been published extensively.  
(Mullin et al., 1997; Peralta Soler et al., 1999;  
Mullin and McGinn, 1988).

Please replace the paragraph at page 7, line 25, over to  
page 8, line 2 of the specification with the following  
substitute paragraph:

There is ~~(an)~~ extensive literature indicating  
that the class of tumor promoters (secondary  
carcinogens) called phorbol esters, can regulate TJ  
permeability and assembly. Phorbol esters have been  
known to increase TJ permeability since the early  
1980s. (Ojakian, 1981; Mullin and O'Brien, 1986). This  
action of phorbol esters was then attributed to PKC  
activation by studies with a number of structurally  
distinct tumor promoting Protein Kinase C (PKC)  
activators such as teleocidin and diacylglycerols.  
(Mullin et al., 1990; Mullin and McGinn, 1988). In  
gastrointestinal cell sheets, phorbol esters likewise  
increase transepithelial permeability. (Hecht et al.,  
1994). PKC has been shown to mediate the effect of  $Ca^{++}$   
on TJ permeability (Tai et al., 1996).

Please replace the paragraph at page 12, line 25, over to  
page 13, line 5 of the specification with the following  
substitute paragraph:

In close collaboration with the Departments of  
General Surgery and Pathology of Lankenau Hospital,  
this research group has been able to demonstrate that  
the tight junctions between epithelia of

adenocarcinomas of human colon are leaky (relative to the tight junctions of epithelia from colon mucosa more than 10 cm distant from the edge of the tumor). The actual conduct of these studies begins with notification to this research group of upcoming colectomy surgeries. It is then necessary to prepare to receive specimens on the day of that patient's surgery, and notify the pathologist on call that day for frozen sections, that a colectomy for adenocarcinoma is forthcoming. An operating room nurse calls the research lab 5 minutes prior to colon removal. The on-call pathologist and a research group member meet in the frozen sections room, and the pathologist determines if tumor tissue and/or normal mucosa could be taken for research purposes. If this is possible, fresh tumor and normal tissue is transported back to the laboratory in Kreb's Ringer Bicarbonate saline at 4°C.

Please replace the paragraph at page 14, lines 1-7 of the specification with the following substitute paragraph:

Salivary amylase can be assayed separately from its pancreatic form by virtue of a specific inhibitor of its activity (Huang and Tietz, 1982). The level of SA in the saliva of the same patients is analyzed by simply analyzing total amylase in sputum samples. SA is surprisingly stable over time in these clinical samples, a factor which aids the accuracy of the tests. Serum is analyzed undiluted. Saliva is diluted 1:1000 in PBS+1% BSA for analysis of SA.